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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/691,928	10/23/2003	Jay A. Goldstein	JAG 100	1611

23579 7590 12/07/2009

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EXAMINER	
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ART UNIT	PAPER NUMBER
1616	

MAIL DATE	DELIVERY MODE
12/07/2009	PAPER

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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/691,928
Filing Date: October 23, 2003
Appellant(s): GOLDSTEIN ET AL.

Michael J. Terapane
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 13 November 2009 appealing from the Office action mailed 14 April 2009.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

No amendment after final has been filed.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

6,075,056	QUIGLEY, Jr. et al.	6-2000
6,238,683	BURNETT et al.	5-2001
5,219,877	SHAH et al.	6-1993

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1. Claims 1 and 8-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Quigley et al. (US 6,075,056).

Quigley et al. disclose a lotion having the following composition: water, the solvent propylene glycol, the humectant glycerin, the emulsifier glyceryl monostrearate, the preservatives benzyl alcohol and sodium benzoate, the base triethanolamine, a steroid from about 0.01 to 0.1 wt.%, preferably betamethasone dipropionate (betamethasone dipropionate lotion is a class 5 lower-mid strength potency steroid at 0.02 wt.%, see column 5, line 31), and the antifungal butenafine HCl (column 11, lines 3-23; Table G). Quigley et al. also discloses the antifungal compounds include terbinafine and naftifine (column 4, lines 4-51). Quigley et al. further disclose that steroids that penetrate the skin cause undesirable side effects (column 1, lines 28-29), and penetration of the epidermis with the test formulations proved to be significantly lower than that shown for Lotrisone formulation (column 18, lines 38-42). Therefore, Quigley et al. disclose a lotion composition comprising all the limitations of the instant claims and discloses the desire to minimize penetration of the steroid through the

epidermis in an attempt to avoid undesirable side effects. Although the composition listed in Table G of Quigley et al. discloses butenafine as the preferred antifungal, the disclosure recites three antifungal agents of particular interest: terbinafine, naftifine and butenafine (col. 3, l. 63 - col. 4, l. 51). Therefore, one of ordinary skill in the art would immediately envisage a composition comprising all the ingredients listed in Table G, except substituting terbinafine or naftifine for butenafine.

2. Claims 1-3, 8-13 and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Burnett et al. (US 6,238,683, published 29 May 2001, same disclosure as EP 1 159 956).

Burnett et al. disclose compositions comprising an antifungal (i.e. ketoconazole and like related imidazole antifungal agents), a steroidal anti-inflammatory (i.e. desonide), a solvent/penetration enhancer (i.e. propylene glycol), a humectant (i.e. glycerin and/or sorbitol), an emollient (stearyl alcohol or cetyl alcohol), dibasic sodium phosphate, PPG-15 stearyl ether, and benzoic acid (abstract; col. 1, ll. 14-22; col. 2, ll. 5-29 and 47-67; col. 3, ll. 1-60; and Tables 1-4). Burnett et al. further disclose that topical compositions known in the prior art comprise an antifungal and steroid have a pH of between 2.5 and 6 (col. 1, ll. 54-58). Burnett et al. further disclose treating *Trichophyton rubrum* (i.e. tinea corporis, tinea cruris and tinea pedis) with the compositions of their invention (col. 7, ll. 14-23).

It is noted that Burnett et al. disclose the required penetration enhancer/solvent selected from the group consisting of alcohol, propylene glycol, or a combination thereof

(col. 2, ll. 47-56), wherein the instant invention requires the composition does not cause the steroids to penetrate the skin and cause undesirable side effects (instant claim 1). However, propylene glycol is a solvent listed in the instant claim 12. Also, Burnett et al. disclose that the compositions of their invention demonstrate targeted delivery of desonide to the skin (cutaneous compartments) with greater amounts of the medicaments in the intended sites of the epidermis and dermis (col. 8, ll. 29-44). Burnett et al. state that the compositions demonstrated positively less permeation through the skin into the receptor that could clinically translate into lower systemic toxicity (col. 8, ll. 45-59). Therefore, even though Burnett et al. refer to the solvent propylene glycol (same as instantly claimed) as a penetration enhancer/solvent, they clarify the desire to prevent permeation of the medicament through the skin and into the receptor, resulting in diminished side effects. Thus, the compositions of Burnett et al. are disclosed not to penetrate through the skin and into the receptor.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham v. John Deere Co., 383 U.S. 1,148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

1. Claims 1-3 and 7-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Quigley et al. (US 6,075,056) as evidenced by the instant specification.

Determination of the scope and content of the prior art

(MPEP 2141.01)

Quigley et al. teach a lotion composition comprising an antifungal, a low-mid strength steroidal anti-inflammatory (0.01 to 0.1 wt.% betamethasone dipropionate lotion), and excipients that don't afford steroidal penetration of the epidermis, as discussed above. Quigley et al. also teach a cream formulation comprising the same excipients as listed in the aforementioned lotion, wherein the steroid is preferably from 0.01 to 0.1 wt.%, and is preferably betamethasone dipropionate (column 7, line 38 through column 8, line 28; Table A).

Ascertainment of the difference between the prior art and the claims

(MPEP 2141.02)

Quigley et al. do not explicitly teach an explicit composition comprising a low to low-medium potency steroidal anti-inflammatory having a structure shown in instant claim 2, nor those selected from the group listed in claim 7. However, Quigley et al. teach desonide cream 0.05% as a suitable steroid anti-inflammatory for use in the present invention (column 5, line 45). Desonide is a species within the generic structure of steroid anti-inflammatory compounds shown in instant claim 2 (instant claims 2-5).

Also, Quigley et al. do not explicitly teach applying the composition two times per day to the affected area. However, Quigley et al. teach that routine experimentation by one of ordinary skill in the art would be able to determine the effective amount of application of the topical composition (column 7, lines 11-24).

Furthermore, Quigley et al. do not teach applying the composition to a child of under 10 years old. However, Quigley et al. teach desonide cream 0.05% as a suitable steroidal anti-inflammatory and the instant specification teaches that desonide is a class 6 non-fluorinated topical corticosteroid which has been available for more than two decades and clinical trials have shown that desonide is effective and safe for treating children having dermatosis or other skin diseases.

Finding of *prima facie* obviousness

Rational and Motivation (MPEP 2142-43)

Therefore, it would have been *prima facie* obvious for one skilled in the art at the time of the invention to use desonide cream 0.05% in the cream formulation taught by Quigley et al. because Quigley et al. teach that desonide cream 0.05% is a suitable steroidal anti-inflammatory for use in combination with an antifungal. One of ordinary skill in the art would have been motivated to use desonide cream 0.05% in the cream formulation of Quigley et al. because desonide is a class 6 non-fluorinated topical corticosteroid which has been available for more than two decades and clinical trials have shown that desonide is effective and safe for treating children having dermatosis or other skin diseases, as evidenced by the instant applications specification. Also, it would have been routine experimentation for a person of ordinary skill in the art to

determine the number of applications of the cream formulation of Quigley et al. in order to achieve desired results in treating fungal diseases.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

2. Claims 1-13 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Burnett et al. (US 6,238,683) in view of Shah et al. (US 5,219,877).

Determination of the scope and content of the prior art

(MPEP 2141.01)

Burnett et al. teach compositions comprising preferably about 0.05 wt.% desonide (col. 3, ll. 45-53) and preferably about 2 wt.% of an imidazole antifungal agent (col. 3, ll. 7-9 and 45-53), wherein the composition does not permeate through the skin, as discussed above.

Ascertainment of the difference between the prior art and the claims

(MPEP 2141.02)

Burnett et al. teach the antifungal agent includes ketoconazole, miconazole, itraconazole, metronidazole, elubiol, and like related imidazole antifungal agents known to those of skill in the art, but do not teach the antifungal agent to comprise clotrimazole as instantly claimed. However, Shah et al. teach formulations suitable for treatment of

tinea capitis, tinea corporis, tinea cruris, and tinea pedis comprising 0.2 to 2.0% w/v of an imidazole antifungal agent, such as clotrimazole, and further comprising an anti-inflammatory steroid including desonide (column 1, lines 6-14; and column 3, lines 43-65). Shah et al. further teach that commercially marketed 1 wt.% clotrimazole exhibits very low permeation rates through skin, and cannot be effectively used for treatment of deep skin fungal infections (column 6, lines 3-34). Thus, the commercially marketed clotrimazole does not permeate through the skin.

Finding of *prima facie* obviousness

Rational and Motivation (MPEP 2142-43)

Therefore, it would have been *prima facie* obvious for one skilled in the art at the time of the invention to use clotrimazole as the imidazole antifungal agent in the compositions of Burnett et al. because Shah et al. teach clotrimazole as a suitable imidazole antifungal for treating tinea capitis, tinea corporis, tinea cruris, and tinea pedis. One would have been motivated to use clotrimazole as the antifungal agent because Burnett et al. teaches the desire to reduce the amount of skin permeation in order to reduce side effects, and Shah et al. teach that commercially marketed 1 wt.% clotrimazole does not permeate through the skin.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

(10) Response to Argument

(I) Rejection of claims 1 and 8-13 under 35 U.S.C. 102(b) as being anticipated by Quigley et al. (US 6,075,056).

Appellants argue on page 12 that the prophetic formulations (Tables A-H) contain the steroid in an amount of 0.01-2.5 wt.%, preferably 0.01-0.1 wt.%. Formulations containing betamethasone dipropionate in these amounts are stated by Quigley to range in potency from Class 1 to Class 5. Thus picking and choosing is required to arrive at formulations within the scope of claim 1.

However, the examiner respectfully argues that Quigley et al. disclose that betamethasone dipropionate is the preferred steroid in the lotion formulations according to Table G (Col. 11, ln. 1-38), and the only betamethasone dipropionate lotion listed in the table on column 4 through column 5 is 0.02% betamethasone dipropionate lotion, which is a low-medium potency steroid. Thus, Quigley et al. clearly anticipate a lotion comprising betamethasone dipropionate wherein the potency of the steroid is within the scope of the instant claims.

Also, it is noted that Quigley et al. claim a topical cream formulation comprising 0.5-5 wt.% antifungal compound, 0.001-2.5 wt.% anti-inflammatory steroid and pharmaceutically acceptable excipients, wherein the steroid is betamethasone, betamethasone dipropionate, fluocinonide, fluocinoline acetonide, hydrocortisone, methylprednisolone, clobetasol, or beclomethasone. Fluocinolone acetonide cream is a low-medium potency steroid at 0.025 wt.%, hydrocortisone is a low potency steroid at

2.5 wt.%, and methylprednisolone at 1 wt.% is a low potency steroid. Therefore, Quigley et al. claim topical formulations comprising low to low-medium potency steroids in combination with an antifungal compound and pharmaceutically acceptable excipients.

It is noted that appellants argue on page 12 that the lotion in Example 10 of Quigley et al. contains 0.064 wt.% betamethasone dipropionate, which is equivalent to the amount of betamethasone dipropionate in Lotrisone™ cream. However, this statement is in direct contradiction to the statement on page 14 wherein appellants state that the carrier (i.e., cream, lotion, gel, ointment, oil, etc.) can alter the potency of the applied steroidal anti-inflammatory and antifungal. Appellants response filed 14 March 2007 exemplifies this by stating that Valisone lotion, 0.1%, Valisone cream/ointment, 0.1%, and Valisone ointment, 0.1%, are all classified in different potency classes. Thus, 0.064% betamethasone dipropionate lotion and 0.064% betamethasone dipropionate cream are not necessarily equivalent because the potency is dependent on the manner in which it is formulated.

(II) Rejection of claims 1-3, 8-13 and 17 under 35 U.S.C. 102(b) as being anticipated by Burnett et al. (US 6,238,683).

Appellants argue on page 13 that Burnett requires the use of a penetration enhancer. However, the examiner respectfully argues that the instant claims state that the composition does not cause the steroids to penetrate the skin ***and*** cause undesirable local side effects. Therefore, the composition can penetrate the skin but

not cause undesirable local side effects, or not penetrate the skin but cause undesirable local side effects and still be within the scope of the instant claims. Also, Burnett et al. disclose the penetration enhancer/solvent to comprise propylene glycol, which is listed in instant claim 12 as being present in the instant invention. Therefore, the instant claims and Burnett et al. both contain propylene glycol. Thus, the disclosure of propylene glycol in Burnett et al. is not outside the scope of the instant claims.

(III) Rejection of claims 1-3 and 7-17 under 35 U.S.C. 103(a) as being unpatentable over Quigley et al. (US 6,075,056).

Appellants argue on page 17 that the examiner has failed to establish a *prima facie* case of obviousness for at least the reasons as discussed above. Therefore, the examiner response above is incorporated herein by reference.

Appellants further argue on page 19 that Quigley et al. teach examples comprising high potency to medium-high potency steroids. Thus one of ordinary skill in the art reading Quigley et al. would be motivated to prepare high or medium-high potency formulations. However, as discussed above, Quigley et al. clearly envisaged lotions comprising betamethasone dipropionate at 0.01 to 0.1 wt.% (col. 11, ln. 1-37), and 0.02 wt.% betamethasone dipropionate lotions are low-medium potency steroids. Also, Quigley et al. claim cream formulations comprising low to low-medium potency steroids (claim 7). Therefore, it would have been *prima facie* obvious for one of ordinary skill in the art to formulate topical compositions according to Quigley et al. comprising low to low-medium potency steroids.

(IV) Rejection of claims 1-13 and 17 under 35 U.S.C. 103(a) as being unpatentable over Burnett et al. (US 6,238,683) in view of Shah et al. (US 5,219,877).

Appellants argue on page 20 that Burnett et al. does not disclose or suggest compositions containing a low to low-medium potency steroidal anti-inflammatory wherein the composition does not cause the steroids to penetrate the skin and cause undesirable local side effects. However, the examiners response above is incorporated herein.

Appellants further argue that Shah et al. teach a preference for mid-potency steroids in view of certain disadvantages of strong and low-potency steroids. As noted by appellants, Shah et al. teach that low potency steroids fail to provide *fast* relief from inflammatory symptoms. However, the examiner respectfully argues that Shah et al. do not teach that low potency steroids are ineffective at providing relief from inflammation, but merely teach that they do not provide *fast* relief from inflammatory symptoms. Also, Shah et al. do not recite deficiencies with low-medium potency steroids.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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Conferees:

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